Compliance in Chronic Noncancer Pain Patients

on Long-Acting Opiates, Short-Acting Opiates, or Non-Opiates

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ABSTRACT

To compare the hypothesis that treatment with short-acting opioids predisposes patients to abuse with the Drug Enforcement Agency's assessment that long-acting opioids have a higher abuse potential, we did a retrospective study in a multi-specialty neuroscience practice to analyze compliance in patients treated for chronic noncancer pain with Schedule II and III opiates and non-opiates. All patients treated for chronic noncancer pain between March 21 and May 6, 2005 were categorized into three groups: Schedule II long-acting opiates, Schedule III short-acting opiates, and non-opiates. Of 140 patients treated with long-acting opiates, 38% were released from treatment for noncompliance with practice protocol. Of 687 patients treated with short-acting opiates, 32% were released. Of 225 patients treated with non-opiates, 30% were released. The DEA assessment of abuse by relative schedule may be a more accurate practice guide than the generally accepted hypothesis that long-acting opiates predispose patients to less misuse or abuse.

KEY WORDS: Pain management, chronic noncancer pain, opiate, noncompliance, substance use disorder.

PURPOSE

The cost of addictive diseases in the United States is staggering. Over 400,000 deaths per year are attributed to nicotine addiction, over 100,000 to alcohol-related illnesses, and nearly 16,000 to illicit drug misuse (1). Although the first incidence of substance use may be voluntary, frequently thereafter use becomes involuntary. It is thought that half of the risk for addictive disorders is genetic (2-4). The lifetime prevalence rate of any substance use or disorder is 49.6% (5). The peak age for beginning drug use is 18 to 20, and most users begin before the age of 30 (6). Early drug use is itself the strongest predictor of misuse, abuse, and dependence (7). The illicit use of drugs is rare among older adults, except among those who abused them in youth (8). The adolescent brain may release more of the euphoric transmitter dopamine in response to addictive substances and may also have less-developed inhibitory neurocircuitry. The National Institutes of Health report that most addiction develops during adolescence, and neuroscience has shown the young brain to be far more vulnerable to addiction than is to the adult brain. Indeed, the 49.6% lifetime prevalence of substance use and the 0.01% risk for addiction among patients receiving opiates for pain indicates that it is much more likely (4,960:1) that a presenting patient will already have tried some substance than that a physician will initiate the disease of opiate addiction (5, 9).

Epidemiological studies of addictive disorders predict a low risk or incidence of opiate addiction in an individual over 30 years of age who does not have a history of abuse or dependence. However, the same science shows a high prevalence of substance use disorders (defined in Table 1), under treatment, early age of onset, polysubstance use, and relapse. All these problems pose significant challenges to the physician treating the chronic noncancer pain patient.

Chronic noncancer pain, which affects more people than any other type, is frequently caused by spinal injuries, post laminectomy syndromes, spinal nerve injury syndromes, spinal cord injuries, degenerative spinal diseases, fibromyalgia, and trauma, all of which are non-terminal and usually not acute conditions. Such pain is the most frequent type a neuroscience physician will see, yet is the most problematic, the most controversial, and the most difficult to manage (10).

Increase in the abuse of opioids is a growing public health problem that should be addressed by identifying causes and sources of diversion without interfering with legitimate medical practice and patient care (11). Non-medical use and abuse of prescription opioids is on the rise in the United States. The illicit use of several widely prescribed opioids has increased more than use of illegal drugs, and the prevalence of prescription opioid abuse appears to be similar to that of heroine and cocaine (12). The legitimate expansion of clinical opioid analgesic use for severe chronic noncancer pain together with the addition of high-dose extended release oral formulations of opioids with good bioavailability has created increased opportunities for the illicit use of these prescribed drugs (13).

Many patients with chronic noncancer pain are moved from short-acting opiates to long-acting opioids administered around the clock to prevent baseline pain. These patients are then given short-acting opioids as supplemental agents for breakthrough pain. This combination is considered one of the ideal treatments for persistent pain (14). Other research suggests there is insufficient evidence to prove that different long-acting opioids are associated with different efficacy or safety profiles and that there is also insufficient evidence to determine whether long-acting opioids as a class are more effective or safer than short-acting opioids (15).

The DEA has scheduled medications as follows: Schedule I substances have no medical purpose and have the highest potential for abuse. Schedule II medications have a high potential for abuse. This category includes some short-acting medications (such as Tylox®, Percocet®, Roxicodone®) and all of the long-acting opiate medications (such as OxyContin®, MS Contin®, Avinza®, Kadian®, and Methadone®). Schedule III medications, which have less potential for abuse, include combination medications (such as hydrocodone and Tylenol®, i.e., Lortab®, Lorcet®, Vicodin®, Norco®). Theoretically, it should take less hydrocodone and Tylenol® than hydrocodone alone to treat the same amount of pain in a patient. The PDR dose limits for Vicodin HP®, Lortab® 7.5mg, and Lortab® 10mg is a maximum daily dose of six tablets per day for an adult (16). Our practice guidelines call for no more than 5 units per day of the above-mentioned Schedule III medications. The patient may use over-the-counter Tylenol® occasionally for breakthrough pain or for acute problems (10).

The hypothesis that long-acting Schedule II opiates are less reinforcing than short-acting (short half-life) opiates would predict a higher rate of compliance in patients being treated with such medications. However, the DEA schedules predict that a short-acting Schedule III opiate has a lower potential for abuse. Thus one would predict that patients treated with the Schedule III opiates should show a higher rate of compliance. The purpose of this paper is to compare noncompliance in patients being treated for chronic noncancer pain by a multi-specialty neuroscience practice with published guidelines and universal precautions for treating chronic noncancer pain (10, 17) in order to explore these diametrically opposed hypotheses and predictions.

METHODS

All patients with chronic (more than three- to six-months) noncancer (non-terminal) pain being treated by a Kentucky multi-specialty neuroscience physician group (eight board-certified

physicians) are subjected to a set of universal precautions designed to assess for substance use disorders. The practice has developed ten useful guidelines for the treatment of chronic non-cancer pain (Table 2) (10). The universal precautions are applied to all noncancer pain patients.

The practice operates five clinics in Kentucky staffed by rotating multi-specialty neuroscience physicians (board certifications in neurosurgery, neurology, neuroimaging, radiology, neuroradiology, pain medicine, anesthesiology, addiction medicine, and musculoskeletal) and approximately 70 employees. The clinics are connected by dedicated T-lines to central Citrix® servers in the Lexington office (intranet) using 200-byte encryption and state-of-the-art firewalls. The intranet is also used to route all calls via voice-over internet protocols (VOIP) to a central call center for triage and improved patient compliance and monitoring. Physicians may access any patient medical record from any exam room in any office location using the real time encrypted T-lines connected to central servers in the Lexington office running Impact® EMR. This technology allowed the authors to access, analyze, and review data generated in multiple locations from a single workstation.

Over the six-week period March 21 through May 6, 2005, all patients treated for chronic noncancer pain were assigned to one of three categories of pain management drug regimen: 1) Schedule II Long-Acting Opiates, 2) Schedule III Short-Acting Opiates, and 3) Non-Opiates. Category assignment was achieved by retrospective analysis of electronic medical records using the search function on Impact® EMR and analyzing individual patients' drug log images and medication regimen. All patients released from practice for noncompliance during this period were assigned to the same three categories by the same retrospective record review.

FINDINGS

Of 140 patients treated primarily with Schedule II long-acting opiates; 53 (38%) were released from treatment for non-compliance. Of 687 patients primarily treated with Schedule III short-acting opiates, 223 patients (32%) were released. Of 225 patients being treated with non-opiates, 67 patients (30%) were released. These results are summarized in Table 4. The most frequent causes of release from this practice are summarized in Table 4 (submitted paper).

DISCUSSION

The results suggest that the hypothesis that long-acting opiates are less reinforcing may not be completely accurate. The practice released a higher proportion of patients on long-acting opiates (38%) than on short-acting opiates (32%) or non-opiates (30%).

These results are similar to those of Manchikanti et al. (18), who found no significant differences in illicit drug use and/or misuse of opioids between patients treated with short half-life hydrocodone and those treated with long half-life Methadone®. Their findings suggest that the use of long-acting opioid formulations by patients with chronic pain does not reduce the risk of drug abuse or improve compliance with medical therapy. Our results may differ somewhat from those of Manchikanti et al. in that we have a different patient clinical mix: they have a pure pain practice in Western Kentucky and we have a multi-specialty neuroscience practice serving Central and Eastern Kentucky. Manchikanti et al have reported that over 90% of their patients are on opiates (18).

Previous research has shown that the primary reasons for patient release in our practice were noncompliance urine drug screen and noncompliant state narcotic monitoring reports (KASPER, Table 4) (10)(submitted paper). Most noncompliant urine drug screens found marijuana (THC), and most noncompliant KASPER reports were due to opiates. Thus, the

finding in this study that we released a higher percentage of Schedule II patients suggests a higher rate of substance use disorders (Table 1) among those released. An estimated 13.7% of non-medical users of prescription opioids have a substance use disorder (19).

Clinicians may be well served by continuing to follow a very conservative approach in treating chronic noncancer pain patients with opioids. Follow the step care approach very carefully and consider moving from Schedule III opioids to Schedule II opiates only when failure occurs with less potent opioids used in combination with non-opioid analgesics or alternative forms of treatment (10, 20). Once a patient is on a long-acting opiate, consider using non-opiate analgesics with techniques such as injective therapies or physical therapies to decrease the total overall dose of opiates (21).

Opiates appear to have their strongest rewarding effects through afferents to the mesolimbic dopamine system. The medium spiny neurons of nucleus accumbens may be viewed as a final common path for drug reward circuitry (9). The current distinction between a habit and an addiction is that an addiction is a compulsive habit maintained despite harmful consequences. This behavior may be caused by opiates stimulating the reward circuits to a greater extent than natural pleasures of life. Total dose of opiate or potency of opiate may be a stronger stimulant of reward circuits than the known potent stimulant of short half-life opiates. Patients with the disease of opiate addiction have an interest in OxyContin largely because its Oxycodone content is much higher than that of short-acting forms of Oxycodone (22).

Pain physicians may underestimate the risk of addiction with Schedule II-type long-acting opiate medication such as OxyContin®. The decision to transfer patients from low-dose short-acting to long-acting opiates may be due to pressures from aggressive marketing practices or patient demands (22, 23). Physicians should be careful to prescribe medications within the

dosing ranges recommended by the Physician's Desk Reference and other resources (24). Once the maximum dose of a short-acting opiate is reached, consider combinations of non-opiates and other alternatives before adding or starting a more potent Schedule II opiate.

The risk of addiction with long-acting opioids has not been studied. The hypothesis that use of long-acting opioids reduces the incidence of prescription drug abuse awaits validation with clinical trials (25). Our results cast doubt on the widely held belief that the ideal treatment for persistent pain is long-acting opioids administered around the clock to prevent baseline pain with the supplemental short-acting opiates for breakthrough pain. Physicians using opioids to treat patients with chronic noncancer pain would be well advised to consider using universal precautions (submitted paper) and to carefully consider when patients should be placed on long-acting opiates.

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Table 1. Definitions/Criteria for Substance Use Disorders

Experimental Use	Short-term random use of one or more drugs motivated by curiosity
Recreational Use	Voluntary and pattern use that occurs in a social setting among friends
Circumstantial Use	Use to cope with a specific problem or situation of a personal or vocational nature
Abuse	Mal-adaptive pattern of use leading to clinically significant distress manifested by one or more of the following occurring at any time in the same 12-month period: • Recurrent use resulting in failure to fulfill major obligations at work, school, or home • Recurrent use in situations that are physically hazardous • Recurrent substance-related legal problems • Continued use despite recurrent substance-related social or personal problems
Dependence (Addiction)	Mal-adaptive pattern of use leading to clinically significant distress manifested by three or more of the following occurring in the same 12-month period: • Tolerance • Withdrawal • Substance taken in larger amounts or over a longer period of time than was intended • Persistent desire or unsuccessful efforts to cut down or control substance use • A great deal of time is spent in activities necessary to obtain the substance • Important social, occupational, or recreational activities are given up or reduced because of substance use • Use is continued despite knowledge of persistent or recurrent physical or psychological problems that is likely to have been caused or exacerbated by the substance

TABLE 2. Universal Precautions: 10 Cs of Chronic Noncancer Pain

C1 – *Continuing Medical Education*	American Academy of Pain Management (Pain Program Accreditation, Am J Pain Management), American Board of Pain Medicine, American Society of Addiction Medicine (J Addictive Dis), Federation of State Medical Boards, SAMHSA, ONDCP, NIDA, DEA, Federal Registrar, www.addictioncme.com, American Pain Society, American Society of Neuroimaging.
C2 – *Consultation*	Pain specialists only treat chronic noncancer pain patients with referral. Primary care physicians should obtain periodic consultation with an appropriate specialist.
C3 – *Comprehensive History*	Always include CAGE-AID questions (include drugs), photo ID, age (most addiction starts before age 30), history of psychiatric illness, drug use/abuse/dependence/conviction/treatment, suicidality. Any angry patient may be trying to manipulate or extort pain medication.
C4 – *Confirmatory physical exam and imaging exam*	Confirmatory physical, review of actual images before prescribing any controlled substance. Drug seekers sometimes purchase "abnormal" radiology reports on the street. Repeat or additional imaging at least annually to exclude occult progressive disease if opiates still required.
C5 – *Contract or consent for treatment*	Every chronic noncancer pain patient must review and sign a contract/consent for treatment with and without controlled substances at every visit. Use consent to educate and define boundaries. No consent, no treatment. Patients must agree to meet at least1 of 3 goals: return to work/school, lower visual analog pain scores, or improved function in activities of daily living.
C6 – *Consider the Alternatives and Adjunctive Measures*	All chronic noncancer pain patients should have tried or be willing to try alternatives and adjunctive measures to minimize or eliminate the overall dose of controlled substances. Use stepped-care with all such patients. Consider combinations of non-controlled medications, home exercise programs, and physical therapy.

TABLE 2. Universal Precautions: 10 Cs of Chronic Noncancer Pain

C7 – *Compliance Measures and Co-morbidities*	Random urine drug screen to confirm the presence of any prescribed controlled substance and rule out illicit drug use. Periodic check of the Kentucky All-Scheduled Prescription Electronic Reporting Program (KASPER) to eliminate doctor shoppers or patients operating in a poly-pharmacy/poly-physician mode. Periodic psychological assessment to assess anxiety and depression.
C8 – *Control*	Prescription pads for controlled substances should specify only one pharmacy, no early refills. The first three letters of the physician's DEA registration number must be handwritten by the physician. All chronic noncancer pain patients should have an individualized drug log and limits on the type and dose of medications.
C9 – *Call blocks*	Do not call in any controlled substance at any time. Any controlled substance prescription requires a face-to-face evaluation.
C10 – *Compassion*	Compassion is getting a patient the right type of treatment. Explain that a noncompliant urine drug screen is not a diagnosis of addiction and refer to a behavioral health specialist, psychiatrist, addiction specialist.

Table 3. Results Summary

Chronic Non-Cancer Pain Management Drug Regimen			
	Schedule II Long-Acting Opiates	Schedule III Short-Acting Opiates	Non-Opiate Pain Management
Total Patients	140	687	225
Released Patients	53	223	67
Percentage	38%	32%	30%

Table 4. 1,405 Released Patients (8/1/03 through 12/1/04)*

Reason for Release	Percent Released
Noncompliant urine drug screen	29%
Noncompliant Kentucky All Schedule Prescription Electronic Reporting System (KASPER)	27%
Failure to keep prescheduled appointments	17%
Other pain management contract/consent for treatment violations	17%
Patient self-release from practice	10%

*from Gilbert, J.W., Wheeler, G.R., Lingreen, R.A., Scheiner, S.J., Sutton, T., Gross, R., Mangione, K., Carter, K., McConnell, M., Evans, B. and Westerfield, G., Universal precautions essential in treating chronic noncancer pain given the high prevalence of substance use in society, submitted to Pain Medicine, 2005